Press release
2 October 2023

Last Patient Out in Phase 3 Study of KP-100IT for the Treatment of Acute Spinal Cord Injury

Kringle Pharma, Inc. (Head office located in Ibaraki, Osaka; President & CEO, Kiichi Adachi; "KRINGLE"), a late clinical-stage biopharmaceutical company, today announces that the last patient has now completed the treatment and follow-up in the Phase 3 clinical trial of KP-100IT, the intrathecal formulation of recombinant human HGF, in patients with acute spinal cord injury. This Phase 3 trial is a nonrandomized, multicenter, confirmatory trial in 25 subjects with severe cervical spinal cord injury. KRINGLE plans to collect and fix all clinical data from this trial for further analysis and evaluation of efficacy and safety. The top-line results are expected to be released in the first half of 2024.

"This clinical trial has been conducted under extremely difficult circumstances due to the COVID pandemic. We would like to express our deepest gratitude to all the patients and their families who participated in the study, as well as the doctors and staff at the clinical trial sites," said Kiichi Adachi, President & CEO of KRINGLE. "There exist huge unmet medical needs in the acute phase of spinal cord injury. The development of effective and safe new drugs is strongly desired. We will evaluate the outcome from the study as soon as possible and begin discussions with the PMDA (Pharmaceuticals and Medical Devices Agency) to apply for regulatory approval. If HGF administration can alleviate some of the disability of patients in the acute phase of spinal cord injury, further functional recovery can be expected through subsequent rehabilitation and/or cell transplantation that is currently under development. We will do our utmost to obtain regulatory approval to deliver the new HGF drug to patients right away."

About Hepatocyte Growth Factor (HGF)

HGF was originally discovered as an endogenous mitogen for mature hepatocytes. Subsequent studies demonstrated that HGF exerts multiple biological functions based on its mitogenic, motogenic, anti-apoptotic, morphogenic, anti-fibrotic, and angiogenic activities, and facilitates regeneration and protection of a wide variety of organs. HGF exerts neurotrophic effects and enhances neurite outgrowth, and the therapeutic effect of HGF on spinal cord injury has been demonstrated in animal models by Professors Hideyuki Okano and Masaya Nakamura at Keio University School of Medicine. Expectations for HGF as a novel therapeutic agent are increasing for spinal cord injury.

About Spinal Cord Injury

Spinal cord injury is caused by trauma, leading to a variety of paralytic or painful symptoms. In descending order of incidence, tripping over, traffic accidents and falls from height are the main causes of spinal damage. Recently, due to the rise in the elderly population, tripping over is becoming an increasingly common cause. In Japan, there are approximately 100,000 to 200,000 chronic spinal cord injury subjects with an incidence of about 6,000 new cases per year*. By appropriate early treatment after the injury and specialized rehabilitation, some degree of functional recovery can be expected, but complex severe symptom, including motor paralysis, muscular spasticity, sensory paralysis, dysfunction of internal organs (rectal and bladder

disorder, thermoregulatory dysfunction, decreased visceral function, decreased respiratory function) may often remain. For these reasons, therefore, there is a strong need for the development of a novel drug.
*Source:
Miyakoshi N et al. Spinal Cord 2021 Jun;59(6):626-634.
Sakai H et al. J Spine Res. 2010 1(1):41-51.

As announced in the news release dated February 20, 2021, KRINGLE launched a collaborative research project with Professors Hideyuki Okano and Masaya Nakamura at Keio University School of Medicine (Located in Tokyo, Japan; President, Kohei Itoh). This research aims to develop next-generation therapies for each stage of spinal cord injury (acute, sub-acute and chronic) by combining iPS cell-derived neural stem/progenitor cells owned by Keio University with HGF developed by KRINGLE. To date, we confirmed remarkable functional recovery in animal models of spinal cord injury and jointly filed the following two patent applications as a result of this collaboration. Please see our news releases on each of these patent applications for details.

- Combination treatment of chronic spinal cord injury, the news release dated March 13, 2023
  https://ssl4.eir-parts.net/doc/4884/ir_material1/202379/00.pdf
- Combination treatment for the acute to sub-acute phase of spinal cord injury, the news release dated September 8, 2023
  https://ssl4.eir-parts.net/doc/4884/ir_material1/213342/00.pdf

About Kringle Pharma, Inc. https://www.kringle-pharma.com/en/
Kringle Pharma is a late clinical-stage biopharmaceutical company established in December 2001 to develop novel biologics based on HGF. Currently, Kringle conducts two Phase III clinical studies, which is the final stage of the drug development, in spinal cord injury and vocal fold scar among other target indications. Kringle's mission is to contribute to societal and global healthcare through the continued research, development, and commercialization of HGF drug for patients suffering from incurable diseases.

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